SEAC

Spongiform Encephalopathy
Advisory Committee

ANNUAL REPORT: 1998/99

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SEAC
Spongiform Encephalopathy Advisory Committee

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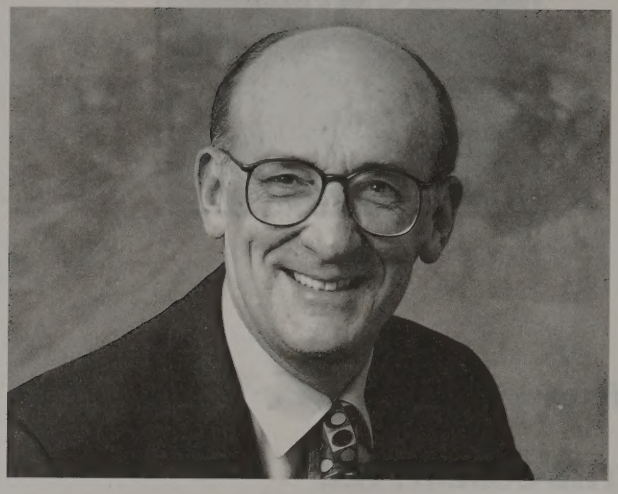
FOREWORD



Welcome to the second Annual Report of the Spongiform Encephalopathy Advisory Committee (SEAC).

Our first Annual Report described the ways in which the recommendations of the 1997 review of SEAC had been carried out and, since then, the work of the Committee has continued to evolve. We began the year by focusing on risk analysis, a theme which became more prominent throughout the following months, during which we also discussed the issues listed for consideration in the 'Future Work' section of our earlier report.

I am indebted to my colleagues on the Committee for their continuing commitment and valuable contributions in tackling complex issues. I would also like to pay tribute to the extensive contribution of the Members who, for various reasons, left the Committee during the year and record our collective sadness at the death of Professor Anne Ferguson.

One procedural change has been the expansion of the SEAC Secretariat to include the Joint Food Safety and Standards Group (JFSSG) as well as the Ministry of Agriculture, Fisheries and Food and the Department of Health. I am grateful to the Secretaries and the support staff in all three branches of the SEAC Secretariat for their support. The Committee continues to be reliant upon access to early research findings and technical briefings on particular issues and I am very grateful to those who throughout the year have helped the Committee in this way.

I hope that you find this report of interest. If you have any comments or suggestions, I would be grateful if you could send these to the SEAC Secretariat.

Professor Sir John Pattison
Chairman

PART I: ABOUT THE COMMITTEE

TERMS OF REFERENCE

1. The Spongiform Encephalopathy Advisory Committee (SEAC) has existed since 1990. The Committee's work increased greatly during 1996 with the identification of a new variant of Creutzfeldt Jakob Disease ('vCJD') and the possibility of a link between this disease and BSE. The Committee was reviewed at the end of that year, and the findings were published in 1997[1]. Following this review the terms of reference of the Committee were redefined as follows:

> "To provide scientifically-based advice to the Ministry of Agriculture, Fisheries and Food, the Department of Health and territorial Departments on matters relating to spongiform encephalopathies, taking account of the remits of other bodies with related responsibilities."

HOW SEAC WORKS

2. SEAC currently meets about 6 times a year and provides scientific advice to Ministers on TSE related matters. Ministers consider SEAC advice in deciding what action to take, and generally publish this advice when announcing their conclusions.

3. The Committee's work is initiated by:

- specific requests for advice from Ministers
- results of research
- requests from the Committee
- specific requests for advice to individual SEAC members.
- the forward business plan contained in the Annual Report.

4. Because of the incomplete scientific understanding of transmissible spongiform encephalopathies (TSEs), it is essential that SEAC has access to early research results and the views of both national and international research councils, academia, individuals, companies, other disciplines and the general public.

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[1] How the review was implemented was covered in the first SEAC Annual Report. Further information on this, and on the historical aspects of the Committee's work and recommendations can be found on the websites of its sponsoring Departments:
MAFF http://www.maff.gov.uk/maffhome.htm
DoH http://www.open.gov.uk/doh/dhhome.htm

MEMBERSHIP

5. The SEAC Review, published in July 1997, identified fields of expertise which should be represented on the Committee. These were epidemiology, microbiology, neurology, neuropathology, veterinary pathology, virology, genetics, veterinary medicine, public health practice, food toxicology/gastro-intestinal immunology and a representative of the public interest. However, it was emphasised that the composition of the Committee should be kept under constant review as more about TSEs becomes known.

6. Six Members left the Committee during the year of this report: three Members retired after an extended period of service and three stood down for personal reasons (2 work related, one due to serious illness). At the close of the year there were twelve remaining Members of SEAC and, given the importance of maintaining a wide field of expertise on the Committee, a selection process based on an open advertisement competition to recruit new Members is underway at the time of writing. Appointments will be made in accordance with the Code of Practice produced by the Commissioner for Public Appointments.

7. New Members are appointed to the Committee on a fixed term basis, usually for three years, with Members normally being asked to serve a maximum of two terms. Members who have served on the Committee before December 1995 are not time limited, although these Members have also been formally appointed on a fixed term basis, up to the end of the 3rd and 6th year respectively. Those Members who have already served more than 6 years are given a fixed appointment for one year, with the possibility of extension in individual cases.

Membership of SEAC during the period covered by this report is given in ANNEX I

CODE OF PRACTICE FOR MEMBERS

8. The Code of Practice drawn up by the Secretariat in 1997 was amended during the year to give specific guidance to members on communications with the media, handling of papers and operation of the Committee in general. The Code is written with regard to the seven principles of public life identified by the Nolan Committee in their report on Standards in Public Life and, in addition to the above, gives specific guidance on publication of work by SEAC Members, conflicts of interest and confidentiality. Copies may be obtained from the SEAC Secretariat.

REGISTER OF MEMBERS' INTERESTS

9. In accordance with the principles of public life identified by the Nolan Committee, details of commercial and non-commercial interests of SEAC

Members which may conflict with their responsibilities as Members of the Committee, are put into the public domain. The register (which will be updated once the recruitment exercise currently underway is completed) is at ANNEX II.

SECRETARIAT

10. At the beginning of the year covered by this report the Secretariat expanded to include the Joint Food Safety and Standards Group (JFSSG), as recommended in the 1997 SEAC Review. Three Secretaries, one each from MAFF, DoH and JFSSG, with support staff, now co-ordinate the work of the Committee and arrange the financing of its activities. (Details of SEAC expenditure can be found in ANNEX III). Addresses for the Secretariat (including website addresses, for further information on the work of each respective Department) can be found at the back of this report.

SUB-GROUPS AND WORKING GROUPS

11. With the approval of Ministers, the Chairman of SEAC can authorise the setting up of *ad hoc* sub-groups to discharge specific tasks. Sub-groups are chaired by SEAC Members, have clear terms of reference and are required to report to the main Committee. There is considerable flexibility about how sub-groups are set up, depending on the issue in question.

12. Expanded use of sub-groups, as recommended in the 1997 SEAC Review, has allowed the Committee to delegate the initial consideration of some of the highly specialised issues which require a substantial input from experts not on the main Committee.

13. During the year work has been carried out by sub-groups on vCJD epidemiology and TSEs in sheep and goats.

ACDP/SEAC Working group

14. In addition to sub-groups, SEAC maintain a joint working group with the Advisory Committee on Dangerous Pathogens (ACDP), which is chaired by the ACDP Chairman. The terms of reference for this group are:

> "To consider the risks from exposure to the agents of transmissible spongiform encephalopathies that may arise as a result of work activities, to develop guidance to minimise such risks and to provide advice as requested by the parent committees (ACDP and SEAC)."

15. During the period of this report the ACDP/SEAC working group met in July and November 1998 and February 1999. The working group also published a report in April 1998 entitled 'Transmissible spongiform

encephalopathy agents: Safe Working and the Prevention of Infection'[2], which offers guidance on working with TSE agents in experimental and clinical settings and is available from the SEAC Secretariat. During the year the working group convened an *ad hoc* sub-group to consider surgical instrument design and TSE contamination. Full membership of the working group is given in ANNEX IV

Epidemiology sub group

16. A SEAC epidemiology sub-group was set up in September 1997, chaired by Professor Peter Smith. It reports jointly to the Chief Medical Officer at the Department of Health and SEAC. It's terms of reference are:

> "To assess the information about the epidemiology of vCJD and develop as far as possible advice on trends in the disease".

17. The sub-group met twice during the year of this report, in May and October 1998, and full membership is given in ANNEX V. SEAC reviewed the work of its epidemiology sub-group in March 1999 and noted that it was still too early to draw conclusions about the likely final size of the outbreak of vCJD from the number or pattern of occurrence of cases reported to date. The view remains that it is likely to be a number of years before it will be possible to make an accurate prediction about the evolution of the vCJD epidemic.

TSEs in sheep and goats sub-group

18. At its meeting in July 1998, SEAC recommended that a sub-group be set up to consider TSEs in sheep and goats and the theoretical possibility that BSE may be present in sheep. The terms of reference, agreed with the Chairman of SEAC, were as follows:

> 'To review the current programme of research and surveillance aimed at quantifying the incidence of scrapie in the UK sheep population, the strains involved and in particular whether or not BSE is present, in order to identify specific areas where further research is needed and where possible, set out a framework of possible approaches'.

19. The sub-group, chaired by Professor Jeffrey Almond, met in September 1998 to review progress of current research and surveillance and make recommendations for further work. Full membership of the sub-group is given in ANNEX VI. A report of the sub-group's conclusions and recommendations for research and surveillance for TSEs in sheep was published in April 1999 and is available from the Secretariat and on the MAFF website[3].

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[2] Available from HMSO, PO Box 276 London SW8 5DT, ISBN 0-11-322166-5,£10

[3] 'SEAC sub-group report: Research and surveillance for TSEs in sheep', published April 1999, available from the MAFF SEAC Secretariat and on the MAFF website http://www.maff.gov.uk/maffhome.htm

OPENNESS

20. The Committee wishes to operate as openly and transparently as possible, and is evolving its practices to that end. The Committee's first Annual Report described the implementation of the 1997 SEAC Review in this respect: SEAC began issuing summaries of its discussions after each meeting and, at the end of last year, published its first Annual Report. (Complete texts of all summaries and advice to Ministers issued by the Committee during the year can be found in ANNEX VII.) During 1998/99 SEAC has taken this further by holding press briefings after each meeting to coincide with the publication of the meeting summaries. These briefings are hosted by the Chairman, who is usually supported by those SEAC members who may have a particular interest in the topics under consideration.

21. During the year the Committee have also moved forward in presenting the scientific advice which is available to them to help them formulate their opinions and for example, published the report of its sub-group on research and surveillance on TSEs in sheep.

22. In addition, the Committee decided in March 1999 to make available a list of published papers distributed to Members since the previous meeting. This list would be published with each meeting summary (see ANNEX VII).

23. SEAC continually look at ways to make such information widely available. Throughout the year the Committee gave consideration to measures to promote further openness without compromising the confidentiality of patient, commercial and scientific information to which it has access and which is crucial to its work. The Committee is keen to encourage a two-way exchange with all who have an interest in its work and welcomes suggestions on how this may be improved. These can be sent to the Secretariat.

PART II: THE WORK OF THE COMMITTEE DURING THE YEAR.

RISK ANALYSIS

24. Traditionally the role of SEAC has been concerned with the assessment, management and communication of risk:

Risk assessment

25. The Committee began the 1998/99 year with a two-day workshop in April on risk assessment. While much of its work is of a sensitive/confidential nature, the Committee are keen to increase awareness of their deliberations, issue advice within the relevant scientific context and to communicate areas of uncertainty.

26. At the April workshop, in addition to Committee Members, scientists and statisticians from such bodies as the Royal Society, the Royal Statistical Society and representatives from a number of European scientific advisory groups also attended. The meeting reviewed the methodology and approaches used in risk analysis and also considered several key biological uncertainties used within risk assessment models. These included:-

- identification of the nature of the agent.
- infectious dose - the amount of the infectious agent that needs to be taken in to induce disease.
- species barrier between animals - the extent to which it is more difficult to transmit a TSE agent between species compared to within species. It was felt that this is the largest single uncertainty. Although experimentally infecting mice and cattle with tissue from BSE infected cattle can provide some clue to the extent of the barrier between the species and experimental infection of transgenic mice carrying the human PrP gene may give relevant data with respect to the cow-human species barrier, it is impossible to define accurately.
- host physiology and oral infectivity. It is unclear how easily and by what route the agent can pass through the gut, particularly at low doses. It is also not known to what extent the host's immune system has any affect on the ability of the agent to establish infection.
- threshold and cumulative dose. It is unclear if low levels of agent can build up following multiple exposure to represent an infectious dose. It is also unclear if a dose over a particular threshold level is required to induce disease.
- subclinical infection. It is unclear if infection can be maintained indefinitely in a subclinical state, and, if such infections exist, whether or not they represent a risk of infection to other animals. If such transmission occurs, it is also unclear if disease will result or the infection will only be sub-clinical.

- variable susceptibility. It is possible that certain individuals or animals may be more susceptible to infection within a population, herd or flock. In particular the genetic factors that are associated with altered susceptibility to infection are still not fully understood.

27. Experiments to resolve some of these uncertainties were discussed. Members also considered potential routes of exposure to the BSE agent, and examined the effect of legislation and other control measures in curtailing the transmission via these routes.

Risk management

28. The Committee's advice to Ministers has also been important in helping to inform the process of risk management. SEAC sometimes provides a bridge between the risk assessment and risk management processes, thus ensuring that Ministers have access to a range of advice and options for action. It is recognised, nevertheless, that in the final analysis decisions are taken at Ministerial level and need to take account of factors other than scientific considerations.

Risk communication

29. The Committee is also involved in the process of risk communication. Summaries are now issued at press briefings after each meeting and the first Annual Report was published last year. In addition, the opinion of the Chairman and individual Members has been sought by the media from time to time on specific issues. As mentioned earlier, SEAC are continually looking at ways to increase the openness of their deliberations.

SUBJECTS CONSIDERED BY THE COMMITTEE DURING THE YEAR:

30. Throughout the year SEAC examined current research within the field of transmissible spongiform encephalopathies. New results from work are presented regularly in the form of published papers and confidential pre-publication drafts. In addition, key results from current research are presented *ad hoc* during Committee meetings.

31. The Committee met seven times between 1 April 1998 and 31 March 1999. During this period SEAC continued to monitor epidemiological data on vCJD and BSE. The number of BSE cases continues to decline, although at a slightly slower rate than predicted, but within the confidence bounds of the predictions. The overall total of confirmed vCJD cases increased to 40.

32. Over the last two years, the Committee has made increasing use of formalised risk assessments. Following on from the assessments of risk from

environmental contamination and possible infectivity from dorsal root ganglia (DRG) and bone marrow in previous years, the Committee has again considered important risk analysis work on the potential risk from human blood and blood products and a review of the risk from beef bones.

Issues addressed by SEAC:
April 1998 - March 1999

A. Protection of public health

- Aetiology of vCJD
- CJD nomenclature
- CJD surveillance
- Prophylactic protection from vCJD- Pentosan Polysulphate
- Human blood and blood products
- Sterilisation/disposal of medical & surgical instruments
- Medicinal product - splenic extract
- Medicinal product - homeopathic medicine
- Safety of milk
- Infectivity in dorsal root ganglia and bone marrow
- Slaughtering methods
- Risk from imported beef products
- Tallow
- The Over Thirty Month cattle slaughter rule

B. Protection of animal health and monitoring

- BSE epidemiology
- Sub-clinical BSE infection
- BSE - maternal transmission
- Feline Spongiform Encephalopathy (FSE)
- TSEs and sheep
- Scrapie surveillance
- Animal feed-use of incinerator ash
- Veterinary medicines

C. Environmental issues

- Disposal of excreta
- Rendering condensate

A. Protection of public health

AETIOLOGY OF vCJD

33. In March 1999 the Committee reviewed its public statement on the link between vCJD and BSE which had originally been issued in March 1996. It concluded that although the link between BSE and vCJD had been shown to be more certain as result of scientific experiments by Professor Collinge and Dr Bruce published in 1997, there was no new information to show how the two diseases were linked. The Committee also felt that after 3 years, and in relation to the current 40 cases as opposed to the 10 identified in March 1996, it could no longer be assumed that all of the cases were necessarily related to exposure prior to 1989 even though no case could be shown to have definitely arisen from exposure after that date. The Committee concluded that in future it could only state that "vCJD was an acquired prion disease caused by exposure to a BSE-like agent."

NOMENCLATURE OF CJD

34. At their meeting in March 1999, SEAC agreed that it would use 'vCJD' in preference to 'nvCJD', in line with current practice in many scientific journals.

CJD SURVEILLANCE

35. In September 1998, the Committee considered a research proposal to survey human tonsil and appendix tissue removed during routine surgery, for the presence of abnormal prion protein. This followed the discovery of abnormal prion protein in tonsils removed from a vCJD patient 8 months before symptoms of disease were seen. SEAC recommended that the study should proceed because examination of these tissues might give some indication of the prevalence of infection with the vCJD agent within the population. However the need for caution when interpreting the results was stressed because the progress of disease in humans is not well defined and the specificity and sensitivity of the techniques in large-scale surveys is not known.

PENTOSAN POLYSULPHATE

36. In January 1999, the Committee considered the use of pentosan polysulphate as a prophylactic treatment to protect against vCJD infection. The Committee agreed that further research to determine the effectiveness of this and similar drugs in controlling the disease agent should be a high priority. However, in the absence of further data on the safety or effectiveness of pentosan, the Committee agreed that they could not recommend its widespread use as a prophylactic prevention against

vCJD. A similar recommendation was made by the Committee on the Safety of Medicines on 10 February.

HUMAN BLOOD AND BLOOD PRODUCTS

37. Previously, SEAC has recommended that a precautionary policy should be adopted to guard against the possible transmission of vCJD through blood transfusion or blood products. The Committee recommended that blood should be leucodepleted if it was practical to do so, pending the results of an assessment of the risk of transmitting vCJD by blood. In June 1998, SEAC considered a preliminary report on the theoretical potential for vCJD to transmit between humans through blood (e.g. via blood transfusion) and blood products. Members agreed that there was considerable uncertainty about whether or not the infectious agent may be present in human blood. However, it was agreed that if infectivity was present in blood it was most likely to be found in lymphocytes, a type of white blood cell. After considering possible management strategies to minimise the potential risk from human to human transmission through blood, the Committee recommended that all blood used for transfusion should undergo leucodepletion to remove white blood cells. The Committee also recommended that further research should be instigated to improve leucodepletion methods and inform the many uncertainties surrounding infectivity in blood.

38. In January 1999, SEAC considered a formal risk assessment on the theoretical exposure to vCJD infectivity in blood and blood products. The Committee agreed that the report provided useful information on the sourcing, processing and uses of human blood and concluded that there was no reason to revise previous advice on blood.

STERILISATION/DISPOSAL OF MEDICAL AND SURGICAL INSTRUMENTS

39. In September 1998, SEAC considered the risk of iatrogenic transmission of vCJD through medical procedures after the discovery of abnormal prion protein in the appendix of a vCJD patient prior to disease onset. Members discussed existing decontamination and sterilisation procedures for surgical instruments and considered possible methods of reducing any potential risk of transmission through surgical instruments, including the feasibility of disposing of instruments after single use. The Committee sent a summary of their discussion to the joint ACDP/SEAC working group for consideration.

40. At the request of the Chief Medical Officer at the Department of Health, SEAC re-examined the possible risks of vCJD transmission associated with surgery at their meeting in March 1999. The Committee considered a risk assessment model

and recommended risk reduction strategies through instrument design and decontamination procedures, especially instrument washing regimes. The Committee also endorsed the conclusions of the joint ACDP/SEAC sub-group on surgical instruments, which recommended urgent research on decontamination of surgical instruments and diagnostic equipment to reduce the risk of prion contamination. SEAC also recommended that discussions should continue with members of the medical profession on the greater adoption of single use of surgical instruments.

MEDICINAL PRODUCT - USE OF SPLENIC EXTRACT

41. In November 1998, SEAC considered the safety of the Kveim test, a diagnostic test for sarcoidosis, derived from human spleen extract (sarcoidosis is an inflammatory disease particularly of the skin, eyes and lungs, of unknown origin). Members recommended that if spleens were used as a raw material for preparations for administration to humans, they should be sourced from a BSE-free country and analysed for the presence of abnormal prion protein before use.

MEDICINAL PRODUCTS - HOMEOPATHIC MEDICINE

42. The use of bovine bone charcoal derived from German cattle in homeopathic medicines was considered at the SEAC meeting in September 1998. After further information was submitted on the farming methods used to rear the cattle at the next meeting in November, it was agreed that because the high temperatures used to produce charcoal would remove any infectivity and the bones were sourced from a BSE-free country, any risk associated with the medicine was likely to be insignificant.

SAFETY OF MILK

43. At the SEAC meeting in April 1998, Members reviewed the possible risk of BSE infectivity in milk. After considering the collection and processing procedures that occur between farm and the consumer, Members agreed that there was no reason to change previous advice on the safety of milk.

BEEF BONES - DRG AND BONE MARROW

44. The Committee had previously considered the infectivity of nervous tissue called dorsal root ganglia (DRG) and bone marrow in December 1997, following preliminary results of experiments that indicated infectivity was present in DRG and that bone marrow may also carry infectivity.

45. In November 1998, SEAC considered the final results from the experiment to assess infectivity in bone marrow. The tests for infectivity of the bone marrow were only positive in the group killed at 38 months after infection with BSE, when clinical disease was evident in the cattle, and not any earlier (2 to 36 months) or later (40 months) after exposure to BSE. The Committee concluded that the positive result at 38 months could not be discounted and may indicate that infectivity in bone marrow occurs occasionally, when clinical signs are apparent and there are already very high levels of infectivity in the central nervous system. Infectivity has not been detected in bone marrow before cattle reach the clinical stage of the disease. All clinically affected cattle (and the majority of infected cattle that are at an advanced stage of incubation) are removed from the food chain when they are slaughtered under the Over Thirty Month rule. The risk to public health from infectivity in the bone marrow of cattle killed for human consumption is therefore likely to be very small and does not have the same significance as DRG.

46. Given that DRG, and potentially bone marrow, could carry infectivity, the Committee reconsidered the risk from these tissues. Although it is still not possible to predict the absolute risk to public health, it was agreed that because of the continuing decline of the BSE epidemic, the risk was reduced in comparison to the previous year. As recommended by SEAC, details of the experiment and the Committee's analysis of the results were made public.

SLAUGHTERING METHODS: STUNNING & PITHING OF CATTLE

47. In November 1998, the Committee considered interim results from a study on common abattoir techniques and their possible association with neural emboli (emboli are small pieces of dislodged tissue that are carried in the bloodstream during the slaughter process). SEAC concluded that the study should be extended to assess if there had been a historical risk from UK slaughter practises. However it was agreed that the number of animals slaughtered for human consumption that might carry infectivity in their brain was now very low and hence the study did not give rise to any concern about the risk of transmitting BSE using current stunning methods.

IMPORTATION OF BOVINE HEADS (CHEEK MEAT)

48. In January 1999, SEAC were asked to consider the risks from cheek meat removed from cattle originating in the Republic of Ireland, a country which has reported cases of BSE. They noted that current legislation states that all heads from UK animals over six months old should be treated as specified risk material and agreed that it would be preferable if all cheek meat imported into the UK came from countries with no incidence of BSE. SEAC recognised that imports are controlled

by EU law, but agreed to summarise their discussion in a letter to the Chief Medical Officer at the Department of Health, which they subsequently did.

TALLOW- FAT MELTING

49. At their meeting in September 1998, the Committee considered the risks associated with 'fat melting', a process which removes edible fat for human consumption from animals less than 30 months old. After considering the raw material and the processes used, SEAC agreed that restrictions on the practice were not necessary and current practice could continue.

OVER THIRTY MONTH SLAUGHTER RULE

50. In November 1998, the Committee began a review of the Over Thirty Month slaughter rule (OTM rule). The Committee considered that any future amendments to the rule should depend on accurately recording the date of birth and movements of all cattle so that each animal could be identified in order to verify its eligibility for human consumption. It was felt that the review of the OTM rule would need to be considered carefully and was likely to take place over several meetings.

51. In March 1999, the Committee considered initial papers on this topic and requested further information to enable it to consider matters further. It agreed however, there was public interest in the review. The Committee supported, and wished to be involved in, any MAFF initiatives to encourage public discussion of the issues involved.

B. Protection of animal health and monitoring

BSE EPIDEMIOLOGY- DECLINE OF THE BSE EPIDEMIC

52. In June 1998, SEAC considered predictions for future cases of BSE. It was noted that a drop in incidence of 20% in comparison to the previous year meant that the epidemic was still declining in line with predictions, although the projected decline had been distorted as a result of the OTMS scheme and the selective cull which removed some animals that may otherwise have gone on to develop clinical disease.

53. In July 1998, SEAC considered possible measures to increase the speed of decline of the BSE epidemic. Members noted that tracing individual cases in the late stages of the epidemic, including the disease status of the mother and the herd, may identify animals suitable for targeted culling. This may allow reconsideration of existing controls i.e. beef on the bone and OTM rule.

SUB-CLINICAL BSE INFECTION

54. Previously, SEAC had considered the theoretical possibility that BSE infectivity could be present in cattle which do not show the signs of clinical disease at any time during their normal lifespan. In April 1998, the Committee considered surveillance protocols and experimental techniques and agreed appropriate research to determine if there was any evidence of sub-clinical BSE infection in the national herd.

55. In June 1998, the Committee considered a draft proposal for a survey of cattle from the over thirty month scheme (OTMS) looking for evidence of sub-clinical BSE infection. They considered possible methods of detecting a hypothetical strain of BSE so far unidentified that may give rise to such a 'sub-clinical' infection. This may differ to pre-clinical BSE i.e. BSE that had not reached the stage when clinical signs develop rather than an animal carrying a latent infection. SEAC concluded that such work should be a high priority, but agreed that further refinements to the diagnostic tests used in the experiment were necessary.

BSE - MATERNAL TRANSMISSION

56. In September 1998, the Committee agreed to a proposal to study further the incidence of BSE in the offspring of BSE affected cows in order to assess the impact of possible maternal transmission on the BSE epidemic.

FELINE SPONGIFORM ENCEPHALOPATHY (FSE)

57. In September 1998, the Committee reviewed the epidemiology of FSE. They agreed that although only 85 cases had been reported in the UK and ascertainment levels may be low, the data were consistent with a food borne source of infection. SEAC agreed that further work on the epidemiology of FSE would be valuable to learn as much as possible from this novel TSE of domestic cats.

BSE AND SHEEP

58. In July 1998, SEAC reviewed experimental work to define the spread of infectivity through individual sheep after experimental exposure to the BSE agent. The Committee acknowledged that the clinical appearance of the disease caused by inoculating sheep with BSE was very similar to scrapie. Because of this, the Committee agreed that surveillance work which examines the nature of all scrapie strains isolated from UK animals should continue as a matter of priority. They recommended that a sub-group be set up to look at this and other issues pertinent to

TSEs in sheep. Key questions for the group were devised. However, SEAC concluded that at present, no action to protect public or animal health, additional to that already taken, was necessary[4].

SCRAPIE SURVEILLANCE

59. In July 1998, SEAC reconsidered the theoretical possibility that BSE could exist in the UK sheep flock. Members reviewed progress on their previous recommendations on scrapie surveillance in sheep and considered methods of analysing strains from cases of natural scrapie to assess if any field cases have similar strain characteristics to those seen in experimental BSE-infected sheep. Questions for the sheep sub-group mentioned above were considered.

ANIMAL FEED

60. In September 1998, the Committee considered a proposal to sell ash derived from the incineration of meat and bone meal (MBM) for inclusion into animal feed. SEAC agreed that this practise contravenes basic principles prohibiting intra-species recycling and agreed that the loophole that could allow this should be closed and the practise prohibited.

VETERINARY PRODUCTS

61. In September 1998, SEAC considered the safety of a veterinary drug which contained bone charcoal of bovine origin used to treat enteric disease. The source of the material was from countries with no history of BSE and the manufacturing process involved very high temperatures that was likely to remove any infectivity. The Committee agreed that the product was safe for use.

C. Environmental issues

DISPOSAL OF EXCRETA

62. In September 1998, SEAC reviewed guidelines for the disposal of experimental animal waste from MAFF's BSE research programme. SEAC reiterated previous advice that following oral dosage the material should be incinerated for the first 28 days post infection, and thereafter all excreta should be composted for a year. In addition, Members agreed that the composted material should not be spread on grazing land used by other cattle but that it could be used as

[4] 'SEAC sub-group report: Research and surveillance for TSEs in sheep', published April 1999, available from the MAFF SEAC Secretariat and on the MAFF website http://www.maff.gov.uk/maffhome.htm

a fertiliser for land on which crops for human and animal consumption were grown.

SPREADING ON LAND OF RENDERING CONDENSATE

63. Previously, the Committee had examined issues related to the waste water 'condensate' produced as a by-product from the rendering process. They had concluded that the risk to human health from spreading the condensate on land was likely to be negligible. In September 1998, the Committee re-examined the risk to animal health after experimental analysis had indicated that the condensate contained ruminant protein of indeterminate origin. Members requested further information on the rendering process and disposal practises involved and agreed to defer any decision until the additional information was presented.

64. In November 1998, after analysing further information, the Committee concluded that the spreading of rendering condensate on farmland should be prohibited. This advice was a precautionary measure to protect cattle which may graze on such land and did not reflect concern about any risk to public health.

Part III - FUTURE WORK

65. There is a continuing need for independent advice to Government on the TSEs. As the BSE epidemic in cattle continues to decline, work is beginning to focus more on the identification and surveillance of vCJD and TSEs in other species, particularly sheep.

66. Public interest in the work of the Committee is understandably high and SEAC will continue to explore ways of opening up their work to a wider audience.

67. During 1999/2000 the Committee will continue to review the epidemiology of TSEs and possible routes of transmission of vCJD. They will also review key research findings as they emerge and deal with any specific issues that are raised. These issues are expected to include medical procedures, the review of the Over Thirty Month slaughter rule which has operated since 1996 and keeping the effectiveness of other existing controls under consideration. The Committee is also expected to review the outcome of scrapie surveillance work and follow up progress with research on TSEs and sheep.

ANNEX I

Membership of SEAC at 31st March 1999

Chairman: Professor Sir John R Pattison

Professor of Medical Microbiology and Vice-Provost of University College, London. Professor Pattison joined SEAC in 1995 and became Chairman in November of that year.

Deputy Chairman: Awaiting appointment

Members:

Professor Adriano Aguzzi

Acting head of the Institute of Neuropathology at the University of Zurich. Professor Aguzzi specialises in neurodegenerative disease research, including prion diseases.

Professor Roy Anderson FRS

Director of the Wellcome Trust Centre for the Epidemiology of Infectious Disease, University of Oxford.

Professor Christopher Bostock

Director of the Institute for Animal Health. Dr Bostock has led the TSE research work at IAH for many years and had been an advisor to SEAC in the past.

Mr Ray Bradley CBE

Veterinary Pathologist and BSE co-ordinator for MAFF until his retirement in 1995.

Professor John Collinge

Professor of Molecular Neurogenetics at Imperial College School of Medicine; Honorary Consultant Neurologist at St Mary's Hospital and the National Hospital for Neurology and Neurosurgery, London.

Dr Peter Goodfellow FRS

Senior Vice President, Biopharmaceutical Research & Development, at Smithkline- Beecham Pharmaceuticals. He was previously Professor of Genetics at Cambridge University.

Professor William D Hueston

Veterinary Epidemiologist and Professor of Veterinary Medicine at the University of Maryland, USA.

Professor Harriet Kimbell MBE

Principal Lecturer at the Guildford College of Law, Deputy Chairman of the Consumers' Association, member of the Polkinghorne Committee on the ethics of genetic modification and food use and the Banner Committee on the ethics of novel breeding techniques and farm animals. Professor Kimbell is SEAC's public interest representative.

Dr Michael Painter

Consultant in Communicable Disease Control, City of Manchester

Dr David B Pepper

Private Veterinary Surgeon (retired), with extensive experience in cattle veterinary practice and slaughterhouse work.

Professor Peter G Smith

Head of Department of Communicable and Tropical Disease Epidemiology, London School of Hygiene and Tropical Medicine.

Departures from SEAC during the year

Six members have left the Spongiform Encephalopathy Advisory Committee in 1998-1999.

Three members retired at the end of 1998:-

Professor Fred Brown - Virologist and chemist
Dr Richard Kimberlin - Consultant on scrapie and related diseases

Dr William Watson - Director of MAFF's Central Veterinary

All retired at the end of extended terms of membership. They had all served on the Committee since its inception in 1990.

In addition three members resigned during the year:-

Professor Robert Will - Consultant Neurologist and Director of the National CJD Surveillance Unit. Professor Will had been a member of SEAC since its inception in 1990 and had been the Committee's deputy Chairman since 1994. He resigned his appointment due to pressure of work at the Surveillance Unit.

Professor Jeffrey Almond - virologist. Professor Almond had completed a three year term on the Committee, but declined an offer of a second appointment after accepted a new post in France. He considered that his obligations to his new job would not enable him to devote enough time to fulfil the commitments a re-appointment to SEAC would require.

Professor Anne Ferguson - gastroenterologist. Professor Ferguson joined the Committee in February 1998, but was forced to resign because of serious illness and, sadly, has since died.

ANNEX II

REGISTER OF MEMBERS' INTERESTS AT 31 MARCH 1999

SEAC MEMBER	COMMERCIAL INTERESTS		NON-COMMERCIAL INTERESTS	
	NAME OF ORGANISATION	NATURE OF INTERESTS	NAME OF ORGANISATION	NATURE OF INTERESTS
Professor Sir John R Pattison (Chairman)	None	None	Medical Research Council	Senior Medical Adviser to the Chief Executive
Prof Dr A Aguzzi	Boehringer Ingelheim	Consultancies on an occasional basis	Swiss National Foundation No: 31-36059.92 3100-040827.94	Principal investigator
	Abbott Laboratories (Chicago)	Support of some laboratory costs e.g. care of mice, instrumentation	Cancer League of the Kanton Zürich	Principal investigator
	Immuno A G (Vienna)	Support of some laboratory costs e.g. care of mice, instrumentation	European Union No. BMHI-CT93-1142	Co- investigator
			National Institutes of Health U.S.A. No 1-ROI-NS33377-01	Co-investigator
			Swiss National Research Program NFP38 & NFP38+	Principal investigator
Professor R M Anderson	Scientific Advisory Boards: - Decode - IMS	 Member of Board Member of Board	The Wellcome Trust	Governor
	IBHSC Ltd	Director		
Professor C J Bostock (Appointed as an expert from the Institute for Animal Health (IAH), a Biotechnology and Biological Sciences Research Council sponsored institute)	Marks and Spencer plc	Share holding	The UK and some overseas Governments	Research contracts with the IAH
	J Sainsbury plc	Share holding	Non-governmental organisations and companies, spanning a wide range of interests including food, agriculture, chemicals and pharmaceuticals. Further details of the customers of IAH can be found on the Institute's Web Site (www.iah.bbsrc.ac.uk)	Research contracts with the IAH
Mr R Bradley	Taylor By-Products	Adviser	Ministry of Agriculture, Fisheries and Food	Adviser
	European Natural Sausage Casings Association	Adviser	Veterinary Laboratories Agency	Adviser
	Meat and Livestock Commission	Adviser	World Health Organisation	Adviser
	National Dairy Council	Adviser	Office International des Epizooties	Adviser
	Jackson and Walker (Attorneys, Counsellors)	Adviser	European Agency for the Evaluation of Medicinal Products	Adviser
	Kraft, Jacobs, Suchard	Adviser	Food and Agriculture Organisation (UN)	Adviser
	National Renderers Association Inc	Adviser	European Commission	Adviser
	Fats and Proteins Research Foundation Inc.	Adviser	National Governments and individuals; especially in Africa, Europe and the Americas	Adviser
	Dr R Öberthur	Adviser	International Natural Sausage Casings Assoc (INSCA) North American Natural Casing Asso (NANCA).	Advisor Advisor
	F D Bisplinghof and Associates Inc	Adviser		

SEAC MEMBER	COMMERCIAL INTERESTS		NON-COMMERCIAL INTERESTS	
	NAME OF ORGANISATION	NATURE OF INTERESTS	NAME OF ORGANISATION	NATURE OF INTERESTS
Professor J Collinge	None	None	Wellcome Trust	Research Grant Holder
			Biotechnology and Biological Sciences Research Council	Research Grant Holder
			Dept. of Health	Research Grant Holder
			European Commission BIOMED programme	Research Grant Holder
			Medical Research Council	Research Grant holder
			Motor Neurone Disease Association	Chairman, Research Advisory Panel
			World Health Organisation	Adviser
Dr P N Goodfellow	SmithKline Beecham Pharmaceuticals	Senior Vice President, Discovery Worldwide. (Head of research worldwide)		
	SmithKline Beecham	Share holding		
	Axys (an American Biotechnology Company)	Share holding		
	Hexagene (A UK Biotechnology Company)	Major share holding		
Professor W Hueston	Mullin, Hoard and Brown (solicitors)	Consultant	Food & Drug Administration (USA)	Adviser
	Cytotherapeutics	Consultant		
	Datascope	Consultant		
Professor H Kimbell	Bass plc	Small share holding		
	Tesco's plc	Small share holding		
Dr M J Painter	None	None	None	None
Mr D B Pepper	The Veterinary Defence Society Ltd	Director and Claims Consultant	None	None
	Pfizer Animal Health (Pfizer Ltd)	Adviser		
	Intervet International BV (Netherlands)	Adviser		
	Intervet UK Ltd	Adviser		
Professor P G Smith	None	None	Department of Health	Grant Holder

(The interests of those members who departed during the year are listed in last year's Annual Report.)

ANNEX III

FINANCE

The cost of running the Committee in 1998/99 was £106,816.00 The breakdown between the departments was as follows:

SEAC Fees and Expenses*	£63,733
Hire of audio equipment & recording	£9584
Hotel accommodation	£9187
Catering(inclusive of VAT)	£2929
Reimbursement of travel and expenses to Committee guests	£2784
Advertising for new members	£2475
Miscellaneous expenditure	£10,179
Total SEAC Expenses	**10,0871**
SEAC Epidemiology Sub Group expenses(including consultancy fees)	£2481
SEAC Sheep Working Group	3464
Total SEAC and Sub-Group expenses	**10,6816**
DEPARTMENT OF HEALTH	
Contribution to SEAC expenses**	£31,500
Epidemiology Sub-group expenses	2481
DH Total	**33981**
MINISTRY OF AGRICULTURE FISHERIES AND FOODS	
Balance of SEAC expenses	69371
Sheep Working Group expenses	3464
MAFF Total	**72835**
TOTAL COST OF SEAC 1998/99:	**£106,816**

* Member fees and entitlements (revised 1.1.98) are as follows

	Chairman	**Members**
Basic fee per day	£148	£122
Exceptional circumstances allowance (payable currently to SEAC members)	£37	£31
Preparation time allowance		
For up to one day's preparatory work	£33	£33
For up to two days' preparatory work	£66	£66

**For the financial year 1998/99, SEAC expenses were paid by MAFF, who requested a contribution from DH at the end of the financial year.

ANNEX IV

MEMBERSHIP OF THE SEAC/ACDP SUB-GROUP AT 31 MARCH 1999

Chairman:

Dr M Crumpton
Chairman - ACDP

Members:

Dr M Painter
Consultant in Communicable Disease Control

Dr J Ironside
National CJD Surveillance Unit

Mr R Clare
Director
Bob Clare Associates

Professor D J Jeffries
The Medical College of St Bartholomew's Hospital, London

Dr T Wyatt
Consultant Clinical Scientist

Dr D Matthews
MAFF

Dr R Owen
Harpenden

Professor P G Smith
London School of Hygiene & Tropical Medicine

Mr R Bradley
Private BSE Consultant

Dr P Jones
Biological & Biochemical Sciences Research Council

Professor S Palmer
Communicable Disease Surveillance Centre Welsh Unit

Mrs T McGuire
General Manager
Lothian NHS Occupational Health Service

Ms J McCulloch
Senior Infection Control Nurse
Royal United Hospital, Bath

Dr D M Taylor
Institute for Animal Health
Neuropathogenesis Unit

ANNEX V

MEMBERSHIP OF THE SEAC EPIDEMIOLOGY SUB-GROUP ON vCJD AT 31 MARCH 1999

Chairman:

Professor P G Smith
London School of Hygiene
& Tropical Medicine

Members:

Professor R G Will
National CJD Surveillance Unit
Edinburgh

Professor C J Bostock
Director
Institute for Animal Health

Professor J Collinge
Prion Disease Group
Imperial College School of Medicine
St. Mary's Hospital, London

Professor R Anderson
Department of Zoology
University of Oxford

Professor N Day
Professor of Public Health & Director of the Institute of Public Health Service

Professor R N Curnow
Department of Applied Statistics
University of Reading

Professor P Willeberg
Division of Ethology & Health
Denmark

Dr G Medley
Dept. Biological Science
University of Warwick

Dr A Hall
London School of Hygiene & Tropical Medicine

Dr C P Farrington
Communicable Disease Surveillance Centre
Public Health Laboratory

Mr J W Wilesmith
Head of Epidemiology Department
Central Veterinary Laboratory
Veterinary Laboratories Agency

ANNEX VI

MEMBERSHIP OF THE SEAC SHEEP SUB-GROUP

Chairman:

Professor J Almond
University of Reading

Members:

Professor A Aguzzi
University of Zurich

Professor R Anderson
University of Oxford

Professor C Bostock
Institute for Animal Health

Dr M Bruce
Institute for Animal Health

Mr M Dawson
Veterinary Laboratories Agency

Dr L Detwiler
Animal and Plant Health Inspection Service, United States Department of Agriculture

Dr C Donnelly
University of Oxford

Dr L Hoinville
Veterinary Laboratories Agency

Dr N Hunter
Institute for Animal Health

Dr R Kimberlin, OBE
Scrapie and Related Diseases Advisory Service

Mr D Pepper
Veterinary Surgeon

Dr A McLean
Institute for Animal Health

Mr J Wilesmith
Veterinary Laboratories Agency

Professor M Woolhouse
University of Edinburgh

ANNEX VII

COMPLETE TEXTS OF SEAC STATEMENTS AND SUMMARIES (1998/1999)

SPONGIFORM ENCEPHALOPATHY ADVISORY COMMITTEE MEETING : 27/28 APRIL 1998

The Spongiform Encephalopathy Advisory Committee (SEAC) met on 27/28 April 1998 at Frensham Pond Hotel, Surrey. The majority of the meeting was devoted to a workshop to review the approaches, methodologies and current level of knowledge of key variables, which are central to the evaluation of risk to humans and animals from exposure to BSE.

Additional scientists from the Royal Society, the Royal Statistical Society, the European Commission's scientific advisory groups, and other risk analysts and statisticians participated in the workshop.

In the first session the meeting considered different approaches to BSE risk assessment and recognised that they now had much in common. The need to consult widely on the models underlying the analyses was noted and it was agreed that an effective way of achieving this was to involve a number of people with relevant expertise. It was agreed that further work on risk analyses conducted on behalf of SEAC should be guided by a group of experts. The main objectives of setting up a risk assessment model were to estimate the impact of measures which might be taken to reduce the risk from any possible exposure and also to enable rapid evaluation of the effects of new information.

In the second session the meeting noted the uncertainty about a number of key biological factors which might be better understood following further research. These included the relative sensitivity of different species to infection with the BSE agent and the roles of the genetics, immune system and gut physiology of the host species in the pathogenesis of the disease. It was noted that there was not yet enough evidence to determine whether there was a threshold level of infectivity required to establish infection in animals or whether an infectious dose could be accumulated.

In session 3 the meeting reviewed the possible routes of human exposure to BSE for the purpose of risk assessment and against which to judge the effect of the measures in place. In session 4 the meeting reviewed BSE infectivity in tissues. It

was noted that detection of infectivity was dependent upon the sensitivity of the bioassay which would be affected by the species barrier factor when a different species was used as recipients. Note was also made of the progress of bioassays of infectivity in tissues from cattle exposed to BSE, using cattle as recipients, where there would be no species barrier. The Committee considered this work was essential but recognised it would take many years to complete due to the long incubation periods involved.

In the final session the participants reviewed the effects of legislation on the control of the epidemic in cattle and protection of public health, noting that the two were closely linked. Without the early legislation (the ruminant feed ban of 1988 and the specified bovine offals ban of 1989 for human food and 1990 for animal feed) the number of cases of BSE in cattle would have continued to rise exponentially. The over thirty month scheme was also noted to have had a major impact in protecting the public from exposure to cattle infected with BSE; more than ninety percent of the animals slaughtered in the last year of incubation before onset of clinical disease were estimated to be removed from the food chain by this measure.

Following the workshop SEAC reviewed aspects of the possible risk of infectivity in milk, including milk processing procedures, the latest scientific evidence and proposals for further research. The discussions were informed by industry experts and scientists with expertise in the field. The Committee concluded that there was no reason to change their previous advice on the safety of milk.

The Committee also noted recent research claiming to show that it was possible for rodents to retain experimental TSE infectivity without exhibiting signs of disease within their life-span. The Committee approved the research proposed to examine whether sub-clinical infection could be detected in cattle.

SEAC
14 May 1998

SPONGIFORM ENCEPHALOPATHY ADVISORY COMMITTEE MEETING : 15 JUNE 1998

The Spongiform Encephalopathy Advisory Committee (SEAC) met on 15 June at the offices of the Ministry of Agriculture, Fisheries and Food, Tolworth.

The Committee conducted its regular review of research findings and the epidemiological information on BSE and CJD.

The number of cases of BSE continues to decline and was down a further 20% from the equivalent period last year.

The total number of definite and probable vCJD cases in the UK was 26.

The Committee reviewed the latest research and assessments of possible risks on human blood and blood products. SEAC presented their advice to Ministers on 17 June 1998.

Members noted a number of procedural improvements to the operation of the Committee and considered future proposals for putting more information in the public domain.

The Committee reviewed a proposal for research into the possibility that a hitherto unrecognised strain of BSE could exist in a sub-clinical form, i.e. cattle could be infected with BSE without ever showing clinical signs of the disease. They considered a number of methods of detecting a sub-clinical strain of BSE and the difficulty of distinguishing such an infection from pre-clinical BSE i.e. BSE that had not reached the stage at which clinical signs of disease were apparent. SEAC concluded that this area of research should be given high priority but noted that further refinements to the diagnostic tests and to the design of the possible studies were necessary.

SEAC
July 1998

SPONGIFORM ENCEPHALOPATHY ADVISORY COMMITTEE MEETING : 30 JULY 1998

The Spongiform Encephalopathy Advisory Committee (SEAC) met at the offices of the Ministry of Agriculture, Fisheries and Food, Tolworth on 30 July 1998.

The Committee conducted its regular review of research findings and epidemiological information on BSE and vCJD.

The number of cases of BSE continues to decline in line with predictions about the decay of the epidemic.

The Committee noted that the total number of vCJD cases in the UK is 27.

SEAC had previously noted that BSE could be transmitted experimentally by mouth to sheep and, in July 1996 and May 1997, had provided advice to Government on precautions which should be taken to protect public health. The Committee considered the theoretical possibility that BSE could exist in the UK sheep flock noting that no evidence of BSE in sheep in commercial UK flocks had so far been found.

The Committee noted that, on the basis of the limited experimental evidence available, the clinical disease caused by inoculating sheep with BSE appeared to be very similar to the natural disease of sheep called scrapie. As in scrapie, infectivity was found in the spleen of sheep experimentally infected with BSE, although no infectivity has been found in the spleen of BSE infected cattle. To distinguish the BSE strain from scrapie strains requires lengthy and expensive post mortem testing of sheep tissue. Such work must continue because, as previously explained (July 1996), finding the BSE strain in the national flock might have important implications for public health.

The Committee noted that valuable preliminary information was emerging from the studies which they had previously recommended. They concluded that additional work was required to determine the extent of scrapie in UK sheep and the strains involved and decided to set up a sub-group to develop further recommendations on this. The Committee agreed that, at present, there was no need to recommend further action to protect public or animal health.

SEAC
August 1998

SPONGIFORM ENCEPHALOPATHY ADVISORY COMMITTEE MEETING : 21 - 22 SEPTEMBER 1998

The Spongiform Encephalopathy Advisory Committee (SEAC) held a two-day meeting at the offices of the Ministry of Agriculture, Fisheries and Food, London on 21 and 22 September 1998.

The Committee conducted its regular review of research findings and epidemiological information on BSE and vCJD.

The number of cases of BSE continues to decline in line with predictions about the decay of the epidemic.

The Committee noted that the total number of vCJD cases in the UK remained at 27. Although there are no indications of an increase in the annual incidence of vCJD it is still too soon to make accurate predictions about the eventual size of the epidemic.

The Committee also reviewed the epidemiological data on feline spongiform encephalopathy. There is only a small number of cases (85 in Great Britain) but the epidemiological data is consistent with a food-borne source of infection. Gathering data is difficult, but the Committee concluded that further epidemiological studies should be initiated to learn as much as possible from this novel TSE of cats.

The Committee discussed the possible risks of transmission of vCJD through medical procedures consequent to the finding of abnormal prion protein in the appendix and tonsils of nvCJD patients. The Committee agreed a summary of their discussions on reducing the risks of iatrogenic transmission which would be made available to inform further consideration of this issue by the joint ACDP/SEAC subgroup which had been set up to look at decontamination procedures and related matters. This working group would take SEAC's views into account in their discussions and report back to the main Committees (ACDP and SEAC).

SEAC also considered the proposal to screen human lymphoid tissue, especially appendix and tonsils, for the presence of abnormal prion protein. While advocating that these studies should proceed they stressed that the results would need to be interpreted with great care. The presence of abnormal prion protein in lymphoid tissue would not necessarily indicate that the patient would later develop clinical neurological disease nor would it indicate the source. Negative results should also be interpreted with caution. Neither the sensitivity of the test, nor the stage of the disease at which abnormal prion protein would be found is known.

The Committee considered and supported a proposal for further studies of cattle which were offspring of BSE affected dams. The study would add to the understanding of the epidemiology of maternal transmission.

SEAC also reviewed proposals for disposal of excreta from large numbers of experimentally infected cattle in the MAFF research programme. They confirmed that after 28 days following oral inoculation the excreta could be composted for a year and then safely used to fertilise arable land and the crops subsequently grown could in principle be used for both human food and animal feed. Excreta from the first 28 days after challenge should be incinerated because if material from the oral inoculation were present in the faeces it would be during this period that the risk would be apparent.

The Committee again reviewed the practice of spreading condensate from rendering plants on farmland. They asked for further information as to exactly what went into the process which produced the condensate to be provided for their next meeting in order to come to a conclusion about the safety of this practice with regard to grazing animals. The Committee had previously concluded that any potential risk to human health from this practice was negligible (SEAC public summary 2 December 1997.)

MEETING WITH THE DORMONT COMMITTEE - 22 SEPTEMBER 1998

On the 22 September SEAC were joined by the Dormont Committee, the French scientific committee on TSEs. The two Committees had previously met in Paris in February 1997. There was a broad exchange of information and views on CJD, BSE and scrapie in France and the UK. There was consensus between the scientists of both Committees on aspects of the epidemiology, genetics, pathogenesis and transmission of these TSEs and in the measures necessary to protect public health. They noted that there were complementary research programmes in place in France and the UK, including collaboration on EU research projects. The Committees agreed to hold a joint meeting again next year.

SEAC
October 1998

SPONGIFORM ENCEPHALOPATHY ADVISORY COMMITTEE MEETING : 9 NOVEMBER 1998

The Spongiform Encephalopathy Advisory Committee (SEAC) met at the offices of the Ministry of Agriculture, Fisheries and Food, Tolworth, on 9 November 1998. The Committee conducted its regular review of research findings and epidemiological information on BSE and nvCJD.

The number of cases of BSE continues to decline in line with predictions about the decay of the epidemic.

The Committee noted that at that time the total number of vCJD cases in the UK was 30. The Committee reviewed the latest experimental results on infectivity in bone marrow and dorsal root ganglia of BSE-affected cattle. The report of the latest scientific assessment has been provided to Ministers and a copy is attached.

The Committee considered preliminary results of research on methods of slaughter

and the possible association with neural emboli (small, possibly even microscopic, pieces of tissue dislodged and carried into the bloodstream during the slaughter process) in the blood. The Committee noted that the research confirmed previous findings that high pressure pneumatic stunners that had not been used in the UK resulted, in some cases, in the presence of emboli in the blood in the large veins draining the head. They concluded that the study of the stunning and pithing methods used in the UK should be extended to evaluate whether the trauma caused by these methods had historically represented any risk of contamination of bovine blood with BSE. The Committee noted that the number of infected cattle that might have infectivity in their brain when slaughtered for human consumption at the present time was very low. Thus the results of this research would not give rise to concern about the risk of transmitting BSE by current practice.

The Committee identified criteria whereby the controls on beef over thirty months of age could be reviewed in the future and hoped to begin to address this at the meeting planned for March 1999. The Committee recognised that this would require careful study and would almost certainly need to be considered over several meetings.

The Committee further considered the practice of spreading rendering condensate on to fields. They noted the procedures associated with the processing of fallen stock. They further noted the difficulty of establishing the origin of any protein found in condensate. They therefore concluded that the spreading of rendering condensate on fields where cattle might graze should be prohibited. The Committee's concerns were related to the risk from BSE to animal rather than human health.

SEAC considered a draft report from its sub-group which had been looking at research and surveillance for TSEs in sheep. It was agreed that a further draft should be prepared incorporating the views of SEAC and those members of the sub-group who had not yet had a chance to comment. It is expected that the final report will indicate the priority of recommendations for further work.

The Committee reviewed the use of human splenic extract in the Kveim test, (a diagnostic skin test used in sarcoidosis). They recommended that where human spleen was used as the raw material for preparations which may be administered to humans, the spleens used should be low risk material, preferably originating from a BSE-free country and screened by immunocytochemistry prior to use.

The Committee agreed to hold a press briefing after each meeting in future, once the public summary of business had been agreed and was ready for publication.

SPONGIFORM ENCEPHALOPATHY ADVISORY COMMITTEE : REPORT TO MINISTERS

A REVIEW OF INFECTIVITY IN BONE MARROW AND DORSAL ROOT GANGLIA IN CATTLE INFECTED WITH BSE

In December 1997 SEAC provided advice to Ministers on the risk to public health from infectivity in dorsal root ganglia and provisional results on infectivity in bone marrow. This report updates that advice taking account of further experimental and epidemiological evidence.

Bone Marrow

Interim results from the BSE pathogenesis experiment in cattle were reported to Ministers in December last year and published in the scientific press in January this year[1] . Further experiments on the infectivity in bone marrow have now been concluded and the results were considered at the SEAC meeting on 9 November. In the experiment conducted by MAFF, groups of cattle were exposed orally to infection with BSE and were then killed sequentially from two to 40 months later. Tissues, including the bone marrow, from the cattle in each group were tested for infectivity by inoculation into mice. The tests for infectivity of the bone marrow were only positive in the group killed at 38 months after infection with BSE, when clinical disease was evident in the cattle, and not at any earlier (2 to 36 months) or later (40 months) time after exposure to BSE[2] .

We agree this positive bone marrow result can be interpreted in three ways:

a) infectivity may occur occasionally in the bone marrow of clinically affected animals;

b) the test is only able to detect infectivity above a certain level and, for BSE infectivity in the bone marrow of cattle, it is operating on the borderline of its

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[1] Preliminary observations on the pathogenesis of experimental bovine spongiform encephalopathy(BSE): an update. GAH Wells et al. Veterinary Record (1998) 142, 103-106.

[2] Personal communication. GAH Wells.

sensitivity;

c) in the case of the group of cattle killed at 38 months after exposure to BSE, the pooled tissue sample was accidentally contaminated at some point during post mortem procedures.

Current evidence does not allow us to determine which of these interpretations is correct. Consequently, our conclusion is that the positive result at 38 months cannot be discounted and may indicate that infectivity in bone marrow occurs occasionally, when clinical signs are apparent and there are already very high levels of infectivity in the central nervous system (brain and spinal cord).

Although BSE and scrapie are not directly comparable (e.g. detectable levels of infectivity in peripheral tissues is a usual occurrence in scrapie but not in BSE in cattle), we have noted that research on scrapie in sheep conducted some years ago demonstrated infectivity in bone marrow of a clinically affected sheep but it was reported as a rare occurrence[3].

Infectivity has not been detected in bone marrow before cattle reach the clinical stage of the disease. All clinically affected cattle are removed from the food chain. So too are the majority of infected cattle that are at an advanced stage of incubation and close to developing clinical disease, when they are slaughtered and destroyed as part of the Over Thirty Months Scheme (OTMS). Consequently the risk to public health from infectivity in the bone marrow of cattle killed for human consumption is likely to be very small and does not have the same significance as infectivity in dorsal root ganglia.

Dorsal Root Ganglia

Infectivity was consistently demonstrated in dorsal root ganglia of cattle in the pathogenesis experiment in the groups of infected cattle killed 32, 36, 38 and 40 months after oral exposure to BSE. At 32 months the animals did not show any clinical signs of disease; these were first seen at 35 months. In some of the dorsal root ganglia transmissions the number of mice infected is very similar to that found with the brain of the same infected cattle, suggesting that high levels of infectivity may be present in the dorsal root ganglia.

Any continuing risk to public health must be evaluated in light of the number of animals likely to be carrying infectivity, their age, how far the disease may have

[3] Natural infection of Suffolk sheep with scrapie virus. WJ Hadlow et al. Journal of Infectious Diseases (1982) 146, 657-664.

progressed when they are slaughtered, and how the carcass is processed for distribution and consumption. Infected animals may have one of three fates; they may be slaughtered for human consumption before the age of 30 months, they may be slaughtered and destroyed as part of the OTMS, or, if they have developed clinical signs, they will be slaughtered and destroyed as a suspect case of BSE. The BSE epidemic in cattle continues to decline. As a result the number of infected animals which are slaughtered for human consumption also continues to decline.

In our advice of December 1997 we referred to the risk from the dorsal root ganglia of animals which, had they lived, would have developed clinical BSE before the age of 38 months. Based on mathematical modelling of the BSE epidemic, we now have estimates[4] of the number of animals under the age of 30 months that will be slaughtered for human consumption during 1999 but would have developed clinical disease within 12 months if they had not been slaughtered. The predictions indicate that in 1999 there will be only 1 or 2 (95% PI* : 0, 5) such infected cattle which will be slaughtered for human consumption. The comparable figure for 1998 was 3 or 4 (95% PI: 0, 8) and for 1997, 5 or 6 (95% PI: 1, 11).

It is possible that small amounts of infectivity might be present in the dorsal root ganglia of animals slaughtered more than 12 months before they would have developed clinical disease had they lived. Current estimates are that in total there will be 43 (95% PI: 25, 66) infected animals which will be slaughtered for human consumption in 1999. The comparable figure for 1998 was 99 (95% PI: 68, 136) and for 1997, 184 (95% PI: 145, 228). We think that infectivity in dorsal root ganglia is likely to increase through the incubation period, so the levels of infectivity will be highest in those animals close to clinical onset. Of the 43 infected animals estimated to be slaughtered in 1999, it is estimated that only 9 or 10 (95% PI: 3, 18) would have developed clinical signs of disease within 2 years if they had not been slaughtered and 22 (95% PI: 11, 37) within 3 years. For comparison we note that the estimated number of infected animals which entered the food chain between 1974 and the introduction of the specified bovine offal ban in 1989 was almost 480,000 (95% PI: 474,000, 819,000), with a further 292,000 (95% PI: 284,000, 303,000) to the end of 1995. In the peak single year 1989 there would have been of the order of 200,000 infected animals slaughtered for human consumption.

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[4] C. Donnelly & N. Ferguson, Personal Communication: Data drawn from the best fitting model described in ' The epidemiology of BSE in cattle herds in Great Britain. II. Model construction and analysis of transmission dynamics' Ferguson N.M. et al 1997 Phil.Trans. R. Soc. Lond. B 352, 803-838.

Conclusions

It is still not known how many humans have become infected with vCJD as a result of exposure to the BSE agent, nor how much BSE infectivity is needed to cause disease. Consequently it is still not possible to predict with any degree of precision the risks to public health from dorsal root ganglia or bone marrow.

However with the continuing decline in the numbers of infected cattle which are slaughtered for human consumption each year any risk from dorsal root ganglia and bone marrow is now less than it was 12 months ago. The pattern of results obtained with bone marrow leads us to conclude that the risk, if any, from this tissue is likely to be very small. With the OTMS in place, we think it likely that the risk from dorsal root ganglia is also very small and negligible in comparison to the possible risk earlier in the epidemic.

It is clearly important that the public are kept informed of these issues and we therefore recommend that the experimental data we have considered and our assessment of its implications are made public.

A further 2 cases of vCJD were confirmed on 12 and 16 November 1998

* 95% prediction intervals, calculated allowing for model fit uncertainty and Poisson variation.

SPONGIFORM ENCEPHALOPATHY ADVISORY COMMITTEE MEETING : 11 JANUARY 1999

The Spongiform Encephalopathy Advisory Committee (SEAC) met at the offices of the Ministry of Agriculture, Fisheries and Food, Tolworth on 11 January 1999.

The Committee conducted its regular review of research findings and epidemiological information on BSE and vCJD.

The Committee noted that the total number of vCJD cases in the UK was 35. The number of cases of BSE continues to decline in line with predictions about the decay in the epidemic.

The Committee had been asked to consider the potential use of Pentosan Polysulphate as a prophylactic against vCJD. Dr. Stephen Dealler attended the Committee, made a presentation and took part in the discussion. Following this the Committee has provided advice to Ministers and a copy is attached.

The Committee had been asked by the Chief Medical Officer of England to consider the risk associated with cheek meat for human consumption removed in Northern Ireland from bovine heads imported from the Republic of Ireland. They noted that a decision of the courts in Northern Ireland meant that the importation of such bovine heads by one specific company for the removal of cheek meat for human consumption had now been permitted pending the outcome of an appeal against this decision to the European Court of Justice. The Committee considered that it would be preferable that cheek meat imported into the UK came only from animals from countries which have no cases of BSE and that bovine heads from which cheek meat was removed within the borders of the UK also came only from such countries. However SEAC recognised that imports are controlled by EU law. With respect to UK cattle over six months old the Committee reaffirmed its advice that the whole head, other than the tongue, should continue to be treated as specified risk material (SRM). The Chairman of the Committee has written to the Chief Medical Officer of England summarising these discussions and conclusions.

The Committee considered a report from Det Norske Veritas (DNV) on the "Assessment of the Risk of Exposure to vCJD Infectivity in Blood and Blood Products". The Committee agreed that because of the many uncertainties preparation of this Report had been a demanding task for DNV and it was difficult to draw any clear conclusions. The Report provided a great deal of useful background information on the sourcing, processing and use of human blood and blood products. The Committee welcomed the intention to publish the report and suggested one or two minor revisions. The Committee saw no reason to revise its earlier precautionary advice to Ministers recommending leucodepletion of blood destined for transfusion.

The Committee, in common with other food safety Advisory Committees, had been asked for its comments in relation to the proposal for an overall framework for the handling of risk analysis, risk management and risk communication across a range of food and food safety issues. The Committee had a preliminary discussion but decided to postpone further discussion until after the BSE Inquiry had reported so that it's findings could be taken into account.

SEAC
January 1999

SPONGIFORM ENCEPHALOPATHY ADVISORY COMMITTEE

ADVICE TO MINISTERS ON THE POSSIBLE USE OF PENTOSAN POLYSULPHATE (PS) AS A PROPHYLACTIC AGAINST vCJD

Pentosan Polysulphate (PS) is a member of a group of complex compounds, number of which have been shown to have an effect on the natural history of scrapie in experimental animal models. The limited experimental evidence suggests the effects are likely to vary according to both the strain of the TSE agent and the species of the host. Therefore, it is difficult to extrapolate the results of scrapie studies in rodents to assess the likely effect of early treatment with this group of compounds on the natural history of vCJD in humans.

In rodent experiments PS has been shown to delay the time at which clinical signs first appear after exposure to the scrapie agent. Experimental evidence also suggests that once the infectious agent has entered the central nervous system PS is unlikely to have any significant effect on development of clinical disease. Consequently, whilst it might be effective during the early stages of infection in preventing progression to the central nervous system it seems unlikely that PS would have a role in the treatment of clinically affected patients or those at the later stages of incubating the disease.

Recent rodent studies had shown the route of administration of PS to be important. There was an effect on the incubation period following intravenous administration but none following oral administration. Further investigation of the kinetics of uptake and subsequent distribution in both animals and humans were needed.

The Committee agreed that there was some scientific evidence that compounds in the PS group might have potential for use as prophylactic agents against vCJD in humans. However, efficacy data were limited and were restricted to animal models using selected strains of the scrapie agent and their applicability to BSE or vCJD was unknown. Safety data currently available on the human use of PS is also restricted to about 10,000 patients treated for unrelated conditions by oral administration.

Further research should be carried out, ideally using BSE and vCJD in experimental animal models, such as transgenic mice carrying the human PrP gene, that may give a better indication of the likely effects of the drug in humans.

In addition, since the peripheral pathogenesis of TSE infection in mice might be significantly different to that in man, studies in primates should also be considered.

We recommend to Ministers that research on this issue should be accorded a high priority. We note that the MRC and DH intend to form a group to consider therapeutic interventions against vCJD, including consideration of PS. We stress the urgency with which this work should be taken forward because we do not know the number of persons who are currently incubating vCJD and consequently the possible risks of transmission of this disease via transfusion from blood donors who are incubating the infection.

Further consideration of the use and safety of PS will need to be given by the Committee on the Safety of Medicines (CSM) and the Committee welcomes the setting up of a joint CSM/SEAC Sub-Group to take this forward.

In the absence of further data on efficacy and safety, SEAC did not consider that it was justified to recommend the wide use of Pentosan as a possible prophylactic against vCJD. In certain circumstances, where there is a tangible risk as a consequence of direct exposure to infectivity (such as an accident in a laboratory), there might be a case for administration of Pentosan. This could be done on a "named patient" basis but this would require more information about the bioavailability and toxicity of Pentosan to be available so that both physician and patient can make a well informed decision. Based on present evidence, there is no justification for the use of Pentosan as a treatment once clinical signs of vCJD are present.

SPONGIFORM ENCEPHALOPATHY ADVISORY COMMITTEE MEETING : 18 MARCH 1999

The Spongiform Encephalopathy Advisory Committee (SEAC) met at the offices of the Ministry of Agriculture, Fisheries and Food, Tolworth on 18 March 1999.

The Committee conducted its regular review of research findings and epidemiological information on BSE and vCJD. The Committee agreed that, "vCJD" should now be used in preference to "nvCJD" in line with current practice in many scientific journals.

The Committee noted that the total number of vCJD cases in the UK was 39.

The Committee reviewed the work of its epidemiology sub-group and noted that it was still too early to draw conclusions about the likely final size of the outbreak of vCJD from the number or pattern of occurrence of cases reported to date.

The number of cases of BSE continues to decline within the 95% confidence limits of the predicted numbers.

The Committee had been asked by the Chief Medical Officer to continue its consideration of the possible risks of vCJD transmission associated with surgery. During the meeting the Committee received a presentation on the risk assessment model of vCJD transmission via surgical instruments developed by the Economics and Operational Research Division of the Department of Health. The Committee commended the usefulness of the model which will allow the effects of new information and possible risk reduction measures to be assessed rapidly.

The Committee was also brought up-to-date with the outcomes of the meetings of the Advisory Committee on Dangerous Pathogens/SEAC Joint TSE Working Group and its sub-group on surgical instruments. SEAC fully endorsed the sub-group recommendation for further urgent work on the decontamination of surgical instruments and diagnostic equipment to reduce the risk of prion contamination. In the meantime SEAC recommended that discussions with surgeons and the Medical Devices Agency on the greater use of disposable instruments for certain surgical procedures should continue.

The Committee reviewed progress in dealing with the BSE epidemic and the measures in place to protect public health. It noted the possibility that the ban on the sale of beef for human consumption from cattle over 30 months old could in due course be amended. It agreed that any change to the Beef Assurance Scheme age limit or eligibility criteria should be addressed as part of any such review. It concluded that further information and analyses would be needed to inform any decision and asked the Secretariat to set this work in hand for the next meeting. The Committee confirmed that this was an issue which would require careful consideration and that it could take several meetings to develop its advice. In the meantime it recognised the public interest in the review of the over thirty month rule and would support and wish to be involved in any MAFF initiatives to encourage public discussion of the issues involved.

The Committee reviewed its public statement on the link between vCJD and BSE which had originally been issued in March 1996. It noted further research had shown that BSE and vCJD were caused by a closely similar prion strain, and concluded that vCJD was an acquired prion disease caused by exposure to BSE or a BSE like agent. When it made its original statement about the first 10 cases in March 1996 the Committee referred to exposure before the SBO ban. After discussion the Committee recognised that not all new cases would necessarily relate to exposure before the SBO ban.

The Committee endorsed the report of its sub-group on sheep, which was published on 14 March.

The next meeting of the Committee will be held on 3 June 1999.

SEAC
14 April 1999

LIST OF SCIENTIFIC PAPERS SUPPLIED TO SEAC MEMBERS BY THE SECRETARIAT BETWEEN 12 JANUARY AND 18 MARCH 1999

Paper by T.Florio, S Thellung, C Amico, M.Robello, M.Salmona, O.Bugiani, F Tagliavini, G Forloni and G Schettini, ' Prion protein fragment 106-126 induces apoptotic cell death and impairment of L-type voltage-sensitive calcium channel activity in the GH3 cell line', published in Journal of Neuroscience Research, 1998, volume 54, pages 341-352;

Abstract by D.Brown, P.Belichenko, M.Jeffrey and J.Fraser, 'Quantification of dendritic spines on pyramidal cells of Scrapie-infected murine and ovine hippocampus using confocal imaging', published in European Journal of Neuroscience, 1998, volume 10, supplement 10, item 122.16;

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Paper by Professor R.G.Will and Dr R.H,Kimberlin 'CJD and the risk from blood or blood products', published in Vox Sanguinis, 1998, volume 75, pages 178-180.

Paper by B Caughey, G.J.Raymond and R.A.Bessen, 'Strain-dependent differences in (-sheet conformations of abnormal prion protein', published in The Journal of Biological Chemistry, 1998, volume 273, issue no 48, pages 32230-32235;

Paper by J.C.Bartz, R.F.Marsh, D.I.McKenzie and J.M.Aiken, 'The host range of chronic wasting disease is altered on passage in ferrets', published in Virology 1998, volume 251, pages 297-301;

Report in WHO Drug Information, 1998, volume 12, No 2, page 81, entitled 'Plasma-derived medicinal products and CJD'; SEAC/INF/56/10

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Commentary by Dr S.M.Gore, 'Mother to-child transmission of nvCJD: uncomfortable question, meagre evidence and subjective beliefs', published in Journal of Epidemiology and Biostatistics, 1998, volume 3, Part 4, pages 375-378;

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Paper by J.Safar and S.B.Prusiner, 'Molecular studies of prion diseases', published in Progress in Brain Research, 1998, volume 117, chapter 29, pages 421-434;

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Note

Copies of SEAC's complete monthly bibliography updates from the secretriat (references only and without abstracts) are published regularly on the MAFF website (address:www.maff.gov.uk/animalh/bse/bse-science/level-3-research.html)

ANNEX VIII

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